



Clinical trial results:

A Phase 3, Randomized, Double-Blind, Multicenter Study Comparing Oral MLN9708 Plus Lenalidomide and Dexamethasone Versus Placebo Plus Lenalidomide and Dexamethasone in Adult Patients With Newly Diagnosed Multiple Myeloma

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-000326-54 |
| Trial protocol | FR BE |
| Global end of trial date | 24 June 2022 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 07 July 2023 |
| First version publication date | 07 July 2023 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | C16014 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01850524 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Takeda |
| Sponsor organisation address | 95 Hayden Avenue, Lexington, MA, United States, 02421 |
| Public contact | Study Director, Takeda, TrialDisclosures@takeda.com |
| Scientific contact | Study Director, Takeda, TrialDisclosures@takeda.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 24 June 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 June 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to provide continued access to ixazomib and/or lenalidomide to participants who are continuing to have clinical benefit and to continue collecting relevant safety data to monitor safety in participants with Newly Diagnosed Multiple Myeloma (NDMM) who are not eligible for stem cell transplant.

Protection of trial subjects:

Each participant signed an informed consent form before participating in the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 29 April 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | France: 262 |
| Country: Number of subjects enrolled | Russian Federation: 5 |
| Country: Number of subjects enrolled | Japan: 59 |
| Country: Number of subjects enrolled | Belgium: 73 |
| Country: Number of subjects enrolled | Korea, Republic of: 31 |
| Country: Number of subjects enrolled | New Zealand: 6 |
| Country: Number of subjects enrolled | United States: 147 |
| Country: Number of subjects enrolled | Canada: 122 |
| Worldwide total number of subjects | 705 |
| EEA total number of subjects | 335 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |

| | |
|---------------------------|-----|
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 19 |
| From 65 to 84 years | 658 |
| 85 years and over | 28 |

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 238 investigative sites in multiple countries from 29 April 2013 to 24 June 2022.

Pre-assignment

Screening details:

Participants with newly diagnosed multiple myeloma were enrolled in 1:1 ratio to receive ixazomib or placebo in addition to the background therapy of Lenalidomide and Dexamethasone (LenDex) in this study.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo + LenDex |

Arm description:

Participants who were randomly assigned to receive placebo matching capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) for the first 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib matching placebo capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months).

| | |
|--|---------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo matching Ixazomib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Ixazomib 4.0 mg capsule single oral dose on Days 1, 8 and 15 for the first 18 cycles (each cycle was of 28 days).

| | |
|--|---------------|
| Investigational medicinal product name | Dexamethasone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22 for the first 18 cycles (each cycle was of 28 days).

| | |
|--|--------------|
| Investigational medicinal product name | Lenalidomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Lenalidomide 25 mg capsules orally on Days 1-21.

| | |
|------------------|-------------------|
| Arm title | Ixazomib + LenDex |
|------------------|-------------------|

Arm description:

Participants who were randomly assigned to receive Ixazomib 4.0 mg capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) for the first 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months).

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ixazomib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Ixazomib 4.0 mg capsule single oral dose on Days 1, 8 and 15 for the first 18 cycles (each cycle was of 28 days). Following cycle 18 participants received 3.0 mg ixazomib capsule as a single oral dose on Days 1, 8 and 15 in each 28-day cycle.

| | |
|--|---------------|
| Investigational medicinal product name | Dexamethasone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22 for the first 18 cycles (each cycle was of 28 days).

| | |
|--|--------------|
| Investigational medicinal product name | Lenalidomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Lenalidomide 25 mg capsules orally on Days 1-21 for the first 18 cycles (each cycle was of 28 days). Following Cycle 18, Participants received lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle.

| Number of subjects in period 1 | Placebo + LenDex | Ixazomib + LenDex |
|---|------------------|-------------------|
| Started | 354 | 351 |
| Intent-to-Treat (ITT) Population | 354 | 351 |
| Completed Study Treatment Per Protocol | 283 | 284 |
| Per Protocol (PP) Population | 293 | 296 |
| Participants With Exposure of ≥ 19 Cycle | 189 | 191 |
| Response-evaluable Population | 347 | 335 |
| Completed | 183 | 178 |
| Not completed | 171 | 173 |
| Withdrawal by Subject | 24 | 22 |
| Lost to follow-up | 5 | 10 |

| | | |
|----------------------|-----|-----|
| Reason not specified | 142 | 141 |
|----------------------|-----|-----|

Baseline characteristics

Reporting groups

| | |
|--|-------------------|
| Reporting group title | Placebo + LenDex |
| Reporting group description: | |
| Participants who were randomly assigned to receive placebo matching capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) for the first 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib matching placebo capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months). | |
| Reporting group title | Ixazomib + LenDex |
| Reporting group description: | |
| Participants who were randomly assigned to receive Ixazomib 4.0 mg capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) for the first 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months). | |

| Reporting group values | Placebo + LenDex | Ixazomib + LenDex | Total |
|--|------------------|-------------------|-------|
| Number of subjects | 354 | 351 | 705 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 73.7 | 73.5 | |
| standard deviation | ± 5.91 | ± 6.53 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 172 | 179 | 351 |
| Male | 182 | 172 | 354 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 14 | 12 | 26 |
| Not Hispanic or Latino | 340 | 337 | 677 |
| Unknown or Not Reported | 0 | 2 | 2 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 2 | 3 |

| | | | |
|---|----------|----------|-----|
| Asian | 52 | 44 | 96 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 1 |
| Black or African American | 13 | 11 | 24 |
| White | 285 | 291 | 576 |
| Unknown or Not Reported | 3 | 2 | 5 |
| Height | | | |
| 'n= 341, 339'. 'n' indicates number of participants available for analysis at baseline | | | |
| Units: centimetre | | | |
| arithmetic mean | 164.7 | 164.3 | |
| standard deviation | ± 10.04 | ± 10.13 | - |
| Body Surface Area (BSA) | | | |
| 'n= 341, 339'. 'n' indicates number of participants available for analysis at baseline. BSA = square root of (height x weight/3600) | | | |
| Units: square metre | | | |
| arithmetic mean | 1.789 | 1.810 | |
| standard deviation | ± 0.2306 | ± 0.2456 | - |
| Weight | | | |
| Units: kilogram(s) | | | |
| arithmetic mean | 70.53 | 72.67 | |
| standard deviation | ± 15.353 | ± 16.995 | - |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Placebo + LenDex |
| Reporting group description: Participants who were randomly assigned to receive placebo matching capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) for the first 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib matching placebo capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months). | |
| Reporting group title | Ixazomib + LenDex |
| Reporting group description: Participants who were randomly assigned to receive Ixazomib 4.0 mg capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) for the first 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months). | |
| Subject analysis set title | Placebo + LenDex (Exposure Up to 18 Cycles) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants who were randomly assigned to receive placebo matching capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) up to 18 cycles (each cycle was of 28 days). | |
| Subject analysis set title | Ixazomib+ LenDex (Exposure Up to 18 Cycles) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants who were randomly assigned to receive Ixazomib 4.0 mg capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) up to 18 cycles (each cycle was of 28 days). | |
| Subject analysis set title | Placebo + LenDex (Exposure \geq 19 Cycles) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants who were randomly assigned to receive placebo matching capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) up to 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib placebo matching capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months). | |
| Subject analysis set title | Ixazomib + LenDex (Exposure \geq 19 Cycles) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants who were randomly assigned to receive Ixazomib 4.0 mg placebo matching capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) up to 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months). | |
| Subject analysis set title | Ixazomib |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants who were randomly assigned to receive Ixazomib 4.0 mg capsules orally once on Days | |

1,8,15 and lenalidomide 25 mg capsules orally on days 1-21 and dexamethasone 40 mg tablets orally on Days 1,8, 15 and 22, during every 28-day cycle for the first 18 cycles.
After Cycle 18 dexamethasone was discontinued and participants continued to receive ixazomib capsule and lenalidomide at reduced doses until progressive disease or unacceptable toxicity, whichever comes first, up to end of study (up to approximately 109 months).

Primary: Progression Free Survival (PFS)

| | |
|--|---------------------------------|
| End point title | Progression Free Survival (PFS) |
| End point description: | |
| PFS was defined as the time from the date of randomization to the date of first documentation of progressive disease (PD) or death due to any cause according to International Myeloma Working Group (IMWG) criteria whichever occurs first. PD required one of the following: Increase of $\geq 25\%$ from nadir in: Serum M-component and/or (the absolute increase must be ≥ 0.5 g/dL); Urine M-component and/or (the absolute increase must be ≥ 200 mg/24 hours); in participants without measurable serum and urine M-protein levels: the difference between involved and uninvolved free light chain (FLC) levels (absolute increase must be > 10 mg/dL); Bone marrow plasma cell percentage: the absolute % must be $> 10\%$; development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas; hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.85 mmol/L). ITT population included all participants who were randomized. | |
| End point type | Primary |
| End point timeframe: | |
| Up to approximately 79 months | |

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 354 | 351 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 21.8 (19.65 to 30.78) | 35.3 (26.45 to 43.70) | | |

Statistical analyses

| | |
|---|--------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
| Number of subjects included in analysis | 705 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.073 ^[1] |
| Method | Log Rank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.676 |
| upper limit | 1.018 |

Notes:

[1] - Log-rank test is stratified by age (< 75 years vs ≥ 75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (< 4 vs ≥ 4) at screening.

Secondary: Overall Survival (OS)

| | |
|-----------------|-----------------------|
| End point title | Overall Survival (OS) |
|-----------------|-----------------------|

End point description:

OS was defined as the time from the date of randomization to the date of death. Participants without documented death at the time of analysis are censored at the date last known to be alive. ITT population included all participants who were randomized. 99999 indicates that Median and Upper limit of Confidence Interval (CI) was not estimable due to censoring of participants as most participants were still alive during last contact.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of randomization to death due to any cause (Up to approximately 9 years)

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|----------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 354 | 351 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 99999 (58.71 to 99999) | 99999 (63.18 to 99999) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--------------------------------------|
| Comparison groups | Ixazomib + LenDex v Placebo + LenDex |
| Number of subjects included in analysis | 705 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | = 0.988 ^[3] |
| Method | Log Rank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.998 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.79 |
| upper limit | 1.261 |

Notes:

[2] - Hazard ratio is based on an Unadjusted Cox's proportional hazard regression model is stratified by age (<75 years vs >=75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs >=4) at screening.

[3] - Log-rank test is stratified by age (<75 years vs >=75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs >=4) at screening.

Secondary: Complete Response (CR) Rate

| | |
|-----------------|-----------------------------|
| End point title | Complete Response (CR) Rate |
|-----------------|-----------------------------|

End point description:

CR rate was defined as the percentage of participants who achieve CR assessed by an IRC relative to the intent-to-treat (ITT) population during the treatment period. Percentage of participants with CR, as assessed by IMWG disease assessment criteria were reported. CR was defined as negative immunofixation of serum and urine along with the disappearance of any soft tissue plasmacytomas and

<5 % plasma cells (PC's) in bone marrow. ITT population included all participants who were randomized.

| | |
|-----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to approximately 9 years | |

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|-----------------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 354 | 351 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 14 | 26 | | |

Statistical analyses

| | |
|---|--------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
| Number of subjects included in analysis | 705 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[4] |
| P-value | < 0.001 ^[5] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.43 |
| upper limit | 3.09 |

Notes:

[4] - Odds ratio and confidence interval are based on logistic regression model with treatment group as categorical predictor variable, age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening as covariates.

[5] - CMH test is stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

Secondary: Pain Response Rate as Assessed by the Brief Pain Inventory- Short Form (BPI-SF) and Analgesic Use

| | |
|---|---|
| End point title | Pain Response Rate as Assessed by the Brief Pain Inventory- Short Form (BPI-SF) and Analgesic Use |
| End point description: | |
| Pain response rate was defined as percentage of participants with pain response. Pain response was defined as the occurrence of at least a 30% reduction from baseline in BPI-SF worst pain score over the last 24 hours without an increase in analgesic use for 2 consecutive measurements > 28 days apart, were reported. Brief Pain Inventory - Short Form (m-BPI-SF) is a participant rated 11-point Likert rating scale ranged from 0 (no pain) to 10 (worst pain imaginable). Percentages are rounded off to the nearest single decimal. ITT population included all participants who were randomized. 'N' indicates overall number of participants with baseline worst pain score ≥4 as assessed by m-BPI-SF. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to approximately 9 years | |

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|-----------------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 195 | 190 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 51.3 | 50.5 | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--------------------------------------|
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
| Number of subjects included in analysis | 385 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[6] |
| P-value | = 0.9195 ^[7] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.98 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.656 |
| upper limit | 1.463 |

Notes:

[6] - Odds ratio > 1 favors Ixazomib+LenDex versus LenDex alone.

[7] - Logistic regression model with prognostic factor: age (<75 years vs ≥75) and ISS (stage I or II vs stage III).

Secondary: Overall Response Rate (ORR)

| End point title | Overall Response Rate (ORR) |
|-----------------------------|---|
| End point description: | ORR was defined as the percentage of participants who achieved CR + partial response (PR) + very good partial response (VGPR) (including sCR) or better relative to the ITT population during treatment period. CR was defined as negative immunofixation of serum and urine along with the disappearance of any soft tissue plasmacytomas and <5 % PC's in bone marrow. PR was defined as ≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥90% along with ≥50% reduction in the size of soft tissue plasmacytomas. VGPR was defined as ≥90% in serum M-component plus urine M-component <100 mg/24. sCR is defined as stringent complete response. Percentages are rounded off to nearest whole numbers. ITT population included all participants who were randomized. |
| End point type | Secondary |
| End point timeframe: | |
| Up to approximately 9 years | |

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|-----------------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 354 | 351 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 80 | 82 | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--------------------------------------|
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
| Number of subjects included in analysis | 705 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[8] |
| P-value | = 0.436 ^[9] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.16 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.79 |
| upper limit | 1.7 |

Notes:

[8] - Odds ratio and confidence interval are based on logistic regression model with treatment group as categorical predictor variable, age (<75 years vs ≥75), ISS(stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening as covariates.

[9] - CMH test is stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

Secondary: Time to Response

| End point title | Time to Response |
|---|------------------|
| End point description: | |
| Time to response was defined as the time from the date of randomization to the first documentation of PR or better, as measured by IMWG criteria. ITT population included all participants who were randomized. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to approximately 9 years | |

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 354 | 351 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 1.87 (1.15 to 1.87) | 1.02 (0.99 to 1.08) | | |

Statistical analyses

| | |
|---|--------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
| Number of subjects included in analysis | 705 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[10] |
| P-value | < 0.001 ^[11] |
| Method | Log Rank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.402 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.185 |
| upper limit | 1.659 |

Notes:

[10] - Hazard ratio is based on an unadjusted Cox's proportional hazard regression model stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

[11] - Log-rank test is stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

Secondary: Duration of Response

| | |
|--|----------------------|
| End point title | Duration of Response |
| End point description: | |
| Duration of response was measured as the time from the date of first documentation of PR or better to the date of first documented progression (PD) for responders, as measured by IMWG criteria. Response-evaluable population was defined as all participants in the ITT population who receive at least 1 dose of any study drug, have measurable disease at baseline, and at least 1 post baseline response assessment assessed by an IRC. Overall number of participants analyzed are the number of responders. 99999 indicates that Upper limit of CI was not estimable as participants without documentation of PD at the date of last response assessment that is stable disease (SD) or better were censored. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to approximately 9 years | |

| | | | | |
|----------------------------------|-----------------------|-----------------------|--|--|
| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 281 | 287 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 37.5 (25.69 to 50.27) | 50.6 (39.98 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP)

| | |
|---|---------------------------|
| End point title | Time to Progression (TTP) |
| End point description: Time to progression was defined as the time from randomization to the date of first documented disease progression. ITT population included all participants who were randomized. | |
| End point type | Secondary |
| End point timeframe: Up to approximately 9 years | |

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 354 | 351 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 26.8 (21.22 to 37.91) | 45.8 (31.84 to 56.25) | | |

Statistical analyses

| | |
|---|--------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
| Number of subjects included in analysis | 705 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[12] |
| P-value | = 0.008 ^[13] |
| Method | Log Rank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.738 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.589 |
| upper limit | 0.925 |

Notes:

[12] - Hazard ratio is based on an unadjusted Cox's proportional hazard regression model stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

[13] - Log-rank test is stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

Secondary: Progression Free Survival (PFS)-2

| | |
|---|-----------------------------------|
| End point title | Progression Free Survival (PFS)-2 |
| End point description: | |
| PFS2 was defined as the time from the date of randomization to the date of documentation of disease progression on the subsequent line of anticancer therapy, as assessed by the investigator in accordance with IMWG criteria, or death due to any cause, whichever occurs first. ITT population included all participants who were randomized. 99999 indicated that Upper limit of CI was not estimable to due insufficient number of participants with events. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to approximately 9 years | |

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 354 | 351 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 52.2 (45.21 to 61.90) | 63.2 (54.70 to 99999) | | |

Statistical analyses

| | |
|---|--------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
| Number of subjects included in analysis | 705 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[14] |
| P-value | = 0.189 ^[15] |
| Method | Log Rank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.859 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.684 |
| upper limit | 1.078 |

Notes:

[14] - Hazard ratio is based on an unadjusted Cox's proportional hazard regression model stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

[15] - Log-rank test is stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

Secondary: Number of Participants With Shifts From Baseline to Worst Value in Eastern Cooperative Oncology Group (ECOG) Performance Score

| | |
|-----------------|---|
| End point title | Number of Participants With Shifts From Baseline to Worst |
|-----------------|---|

End point description:

Eastern Cooperative Oncology Group (ECOG) scale score ranged from 0 to 5, where 0 indicated normal activity and 5 indicated death. The data is reported for those categories where at least 1 participant had worst post-baseline value for each ECOG score. Safety population is defined as all participants who receive at least 1 dose of any study drug. 'N' indicates overall number of participants available for analysis.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to approximately 9 years

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|---|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 344 | 340 | | |
| Units: participants | | | | |
| Baseline Score 0, Post-Baseline Score 0 | 23 | 23 | | |
| Baseline Score 0, Post-Baseline Score 1 | 57 | 52 | | |
| Baseline Score 0, Post-Baseline Score 2 | 20 | 23 | | |
| Baseline Score 0, Post-Baseline Score 3 | 2 | 10 | | |
| Baseline Score 1, Post-Baseline Score 0 | 1 | 1 | | |
| Baseline Score 1, Post-Baseline Score 1 | 96 | 104 | | |
| Baseline Score 1, Post-Baseline Score 2 | 72 | 57 | | |
| Baseline Score 1, Post-Baseline Score 3 | 18 | 9 | | |
| Baseline Score 1, Post-Baseline Score 4 | 6 | 4 | | |
| Baseline Score 2, Post-Baseline Score 1 | 12 | 8 | | |
| Baseline Score 2, Post-Baseline Score 2 | 28 | 35 | | |
| Baseline Score 2, Post-Baseline Score 3 | 7 | 11 | | |
| Baseline Score 2, Post-Baseline Score 4 | 2 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

| | |
|-----------------|---|
| End point title | Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) |
|-----------------|---|

End point description:

An AE was any untoward medical occurrence in a participant administered a medicinal investigational drug. The untoward medical occurrence does not necessarily have to have a causal relationship with treatment. An SAE is any untoward medical occurrence that results in death; is life-threatening; requires inpatient hospitalization or prolongation of present hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect or is a medically important event that may not be immediately life-threatening or result in death or hospitalization, but may jeopardize the participant or may require intervention to prevent one of other outcomes listed in definition above, or involves suspected transmission via a medicinal product of an infectious agent. Safety population= participants who receive at least 1 dose of any study drug. Data for safety is summarized as per duration of exposure to study treatment (exposure up to 18 cycles; exposure ≥19 cycles)

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of randomization through 30 days after the last dose of study drug up to end of study (up to approximately 9 years)

| End point values | Placebo + LenDex (Exposure Up to 18 Cycles) | Ixazomib+ LenDex (Exposure Up to 18 Cycles) | Placebo + LenDex (Exposure ≥19 Cycles) | Ixazomib + LenDex (Exposure ≥19 Cycles) |
|-----------------------------|--|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 160 | 163 | 189 | 191 |
| Units: participants | | | | |
| TEAEs | 160 | 163 | 189 | 191 |
| SAEs | 105 | 119 | 119 | 125 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Serum Chemistry and Hematology Laboratory Values Based on Treatment-emergent Adverse Events (TEAEs)

| | |
|-----------------|--|
| End point title | Number of Participants With Abnormal Serum Chemistry and Hematology Laboratory Values Based on Treatment-emergent Adverse Events (TEAEs) |
|-----------------|--|

End point description:

Laboratory values assessment included serum chemistry and hematology. Serum chemistry assessment - blood urea nitrogen(BUN), creatinine, bilirubin(total), urate, lactate dehydrogenase, phosphate, albumin, alkaline phosphatase(ALP), aspartate aminotransferase(AST), alanine aminotransferase(ALT), glucose, sodium, potassium, calcium, chloride, carbon dioxide(CO2), magnesium, thyroid stimulating hormone(TSH). Hematology assessment - hemoglobin, hematocrit, platelet(count), leukocytes with differential neutrophils(ANC). Participants with abnormal serum chemistry and hematology values reported as TEAEs are reported. TEAEs: events that occurred after administration of first dose of any agent in study drug regimen and through 30 days after last dose of any agent in study drug regimen. Safety population: participants who receive at least 1 dose of any study drug. Data for safety is summarized as per duration of exposure to study treatment(exposure up to 18 cycles; exposure ≥19 cycles).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of randomization through 30 days after the last dose of study drug up to end of study (up to approximately 9 years)

| End point values | Placebo + LenDex (Exposure Up to 18 Cycles) | Ixazomib+ LenDex (Exposure Up to 18 Cycles) | Placebo + LenDex (Exposure ≥19 Cycles) | Ixazomib + LenDex (Exposure ≥19 Cycles) |
|-----------------------------|--|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 160 | 163 | 189 | 191 |
| Units: participants | | | | |
| Hypokalaemia | 16 | 33 | 33 | 39 |
| Blood creatinine increased | 9 | 6 | 12 | 16 |

| | | | | |
|--|----|----|----|----|
| Hypophosphataemia | 2 | 9 | 3 | 9 |
| Hypomagnesaemia | 8 | 6 | 11 | 15 |
| Hyponatraemia | 7 | 10 | 8 | 7 |
| Hyperglycaemia | 4 | 7 | 16 | 6 |
| Hypocalcaemia | 13 | 6 | 12 | 4 |
| Hyperkalaemia | 3 | 7 | 3 | 3 |
| Alanine aminotransferase increased | 1 | 1 | 4 | 10 |
| Iron deficiency | 2 | 1 | 2 | 7 |
| Hypercalcaemia | 6 | 2 | 1 | 5 |
| Creatinine renal clearance decreased | 2 | 1 | 7 | 4 |
| Hypoalbuminaemia | 5 | 2 | 1 | 3 |
| Aspartate aminotransferase increased | 1 | 0 | 3 | 5 |
| Hyperuricaemia | 2 | 2 | 1 | 2 |
| Anaemia | 57 | 53 | 52 | 58 |
| Thrombocytopenia | 15 | 34 | 14 | 24 |
| Neutropenia | 36 | 15 | 48 | 39 |
| Neutrophil count decreased | 11 | 5 | 13 | 18 |
| Platelet count decreased | 6 | 6 | 4 | 15 |
| Lymphopenia | 0 | 7 | 2 | 4 |
| Febrile neutropenia | 5 | 7 | 2 | 2 |
| Leukopenia | 3 | 6 | 4 | 2 |
| International normalised ratio increased | 1 | 4 | 0 | 4 |
| Pancytopenia | 2 | 3 | 1 | 2 |
| Iron deficiency anaemia | 1 | 1 | 1 | 4 |
| White blood cell count decreased | 5 | 1 | 3 | 2 |
| Lymphocyte count decreased | 1 | 2 | 3 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health-Related Quality of Life (HRQOL) Measured by European Organisation for Research and Treatment of Cancer-Quality of Life Questionnaire (EORTC-QLQ)-C30 Scale Total Score

| | |
|-----------------|---|
| End point title | Change From Baseline in Health-Related Quality of Life (HRQOL) Measured by European Organisation for Research and Treatment of Cancer-Quality of Life Questionnaire (EORTC-QLQ)-C30 Scale Total Score |
|-----------------|---|

End point description:

EORTC-QLQ-C30 scale (30 items) was used to assess HRQOL. Subscale with individual items: physical functioning items 1-5, role functioning items 6-7, emotional functioning items 21-24, cognitive functioning items 20, 25, social functioning items 26-27, quality of life items 29-30, fatigue items 10, 12, 18, nausea and vomiting items 14-15, pain items 9, 19, dyspnoea item 8, insomnia item 11, appetite loss item 13, constipation item 16, diarrhoea item 17, financial difficulties item 28. Raw scores were converted into scale scores ranging from 0 to 100. Functional scales and global health status (GHS) scale: higher scores = better HRQOL. Symptom scales: lower scores = better HRQOL. Positive change in functional and global health status scale = improvement; negative change for symptom scales = improvement. ITT population. 'N' indicates overall number of participants available for analyses. 'n' indicates number of participants available for analysis at given timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to approximately 9 years

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|--|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 353 | 351 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| GHS/QOL Baseline (n= 352, 351) | 55.2 (± 23.53) | 56.4 (± 23.66) | | |
| GHS/QOL End of Treatment (EOT) (n= 220, 217) | -2.2 (± 26.03) | -4.1 (± 29.48) | | |
| Physical Functioning: Baseline (n= 353, 350) | 60.0 (± 28.73) | 61.4 (± 27.96) | | |
| Physical Functioning: EOT (n= 223, 217) | 1.7 (± 26.81) | 0.3 (± 28.23) | | |
| Role Functioning: Baseline (n= 352, 350) | 54.9 (± 36.52) | 56.5 (± 36.60) | | |
| Role Functioning: EOT (n= 223, 217) | -0.3 (± 36.25) | -1.8 (± 36.74) | | |
| Emotional Functioning: Baseline (n= 353, 351) | 73.5 (± 23.09) | 72.6 (± 24.84) | | |
| Emotional Functioning: EOT (n= 222, 217) | -2.4 (± 21.70) | -0.5 (± 24.35) | | |
| Cognitive Functioning: Baseline (n= 353, 351) | 77.8 (± 22.97) | 78.3 (± 25.92) | | |
| Cognitive Functioning: EOT (n= 222, 217) | -3.2 (± 25.14) | -5.1 (± 24.70) | | |
| Social Functioning: Baseline (n= 351, 351) | 69.1 (± 32.54) | 69.5 (± 33.01) | | |
| Social Functioning: EOT (n= 220, 217) | -2.9 (± 31.56) | -2.5 (± 36.57) | | |
| Fatigue: Baseline (n= 353, 350) | 44.6 (± 28.30) | 40.8 (± 27.69) | | |
| Fatigue: EOT (n= 223, 218) | -2.3 (± 27.75) | 4.5 (± 31.04) | | |
| Pain: Baseline (n= 353, 351) | 45.6 (± 34.04) | 42.5 (± 33.51) | | |
| Pain: EOT (n= 225, 218) | -5.5 (± 33.77) | -3.5 (± 34.55) | | |
| Nausea and Vomiting: Baseline (n= 353, 350) | 7.1 (± 15.75) | 8.1 (± 18.49) | | |
| Nausea and Vomiting: EOT (n= 224, 218) | -0.5 (± 19.80) | 1.6 (± 25.22) | | |
| Dyspnoea: Baseline (n= 352, 350) | 26.2 (± 30.25) | 24.0 (± 29.35) | | |
| Dyspnoea: EOT (n= 222, 217) | -3.6 (± 30.86) | 2.8 (± 33.83) | | |
| Insomnia: Baseline (n= 353, 350) | 30.3 (± 30.31) | 34.3 (± 32.20) | | |
| Insomnia: EOT (223, 217) | -1.5 (± 35.06) | -1.1 (± 36.06) | | |
| Appetite Loss: Baseline (n= 353, 350) | 25.4 (± 33.14) | 25.5 (± 33.04) | | |
| Appetite Loss: EOT (n= 223, 218) | -1.2 (± 37.42) | 3.4 (± 38.65) | | |
| Constipation: Baseline (n= 352, 351) | 25.9 (± 32.94) | 24.9 (± 32.19) | | |
| Constipation: EOT (n= 222, 218) | -7.1 (± 39.03) | -5.7 (± 35.83) | | |
| Diarrhoea: Baseline (n= 352, 351) | 8.2 (± 19.45) | 6.7 (± 16.58) | | |
| Diarrhoea: EOT (n= 221, 217) | 10.7 (± 27.72) | 18.3 (± 31.73) | | |
| Financial Difficulties: Baseline (n= 352, 351) | 12.5 (± 24.04) | 12.3 (± 24.03) | | |
| Financial Difficulties: EOT (n= 220, 216) | 2.0 (± 27.42) | 0.8 (± 25.61) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HRQOL Measured by EORTC-QLQ-MY20 Scale

| | |
|-----------------|--|
| End point title | Change From Baseline in HRQOL Measured by EORTC-QLQ-MY20 Scale |
|-----------------|--|

End point description:

EORTC QLQ-MY20 was a validated questionnaire to assess the overall quality of life in participants with multiple myeloma. The scale has 20 questions. Subscale and individual items include future perspective items 18-20, body image item 17, disease symptoms items 1-6, side effects of treatment items 7-16. Raw scores are averaged, and transformed to 0-100 scale, where higher score is better quality of life. Positive change indicates improvement. ITT population included all participants who were randomized. 'N' indicates overall number of participants available for analyses. 'n' indicates the number of participants available for analysis at the given timepoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to approximately 9 years

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|--|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 352 | 350 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Disease Symptoms: Baseline (n= 352, 350) | 30.3 (± 23.76) | 29.2 (± 22.97) | | |
| Disease Symptoms: EOT (222, 215) | -3.1 (± 20.74) | -5.3 (± 22.44) | | |
| Side-Effects: Baseline (352, 350) | 18.0 (± 14.53) | 17.6 (± 15.04) | | |
| Side-Effects: EOT (n= 222, 214) | 1.7 (± 14.52) | 3.3 (± 15.91) | | |
| Body Image: Baseline (n= 346, 346) | 81.7 (± 27.67) | 81.2 (± 29.11) | | |
| Body Image: EOT (n= 215, 207) | -7.8 (± 31.93) | -2.3 (± 29.66) | | |
| Future Perspective: Baseline (n= 350, 349) | 57.3 (± 25.95) | 55.0 (± 28.47) | | |
| Future Perspective: EOT (220, 211) | 4.4 (± 24.85) | 6.0 (± 25.69) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OS in High-risk Population Carrying Del(17p), t(4;14), or t(14;16) Mutations

| | |
|-----------------|--|
| End point title | OS in High-risk Population Carrying Del(17p), t(4;14), or t(14;16) Mutations |
|-----------------|--|

End point description:

OS was defined as the time from the date of randomization to the date of death, as assessed in high-risk population carrying del(17p), t(4;14), or t(14;16) mutations. High risk category includes t(4;14), t(14;16), or del(17) abnormalities. ITT population included all participants who were randomized. 'N' indicates overall number of participants from the high-risk category. 99999 indicated that upper range of CI was not estimable due to insufficient number of participants with events.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of randomization to death due to any cause (Up to approximately 9 years)

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 63 | 60 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 43.1 (33.84 to 57.82) | 39.0 (25.43 to 99999) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--------------------------------------|
| Statistical analysis description: | |
| OS in High-risk Population Carrying Del(17p), Amp(1q21), t(4;14), or t(14;16) Mutations | |
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[16] |
| P-value | = 0.662 ^[17] |
| Method | Log Rank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.118 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.678 |
| upper limit | 1.845 |

Notes:

[16] - Hazard ratio is based on an unadjusted Cox's proportional hazard regression model stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

[17] - Log-rank test is stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

Secondary: PFS in High-risk Population Carrying Del(17p), t(4;14), or t(14;16) Mutations

| | |
|-----------------|---|
| End point title | PFS in High-risk Population Carrying Del(17p), t(4;14), or t(14;16) Mutations |
|-----------------|---|

End point description:

PFS was defined as the time from the date of randomization to the date of first documentation of progressive disease based on central laboratory results and IMWG criteria as evaluated by an independent review committee (IRC) or death due to any cause, whichever occurs first, as assessed in high-risk population carrying del(17p), t(4;14), or t(14;16) mutations. ITT population included all participants who were randomized. 'N' indicates overall number of participants from the high-risk category.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to approximately 9 years

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 63 | 60 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 17.5 (12.12 to 20.30) | 22.4 (12.16 to 42.84) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|--|--------------------------------------|
| Statistical analysis description: PFS in High-risk Population Carrying del(17p), t(4;14), or t(14;16) Mutations | |
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[18] |
| P-value | = 0.271 ^[19] |
| Method | Log Rank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.466 |
| upper limit | 1.24 |

Notes:

[18] - Hazard ratio is based on an unadjusted Cox's proportional hazard regression model stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

[19] - Log-rank test is stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

Secondary: Percentage of Participants With MRD-Negative Status as Assessed by Flow Cytometry

| End point title | Percentage of Participants With MRD-Negative Status as Assessed by Flow Cytometry |
|--|---|
| End point description: The absence of minimal residual disease (MRD negativity) was tested in all participants who achieve a CR and maintained it until Cycle 18, using bone marrow aspirates. Response-evaluable population includes all participants in the ITT population who receive at least 1 dose of any study drug, have measurable disease at baseline, and at least 1 post baseline response assessment assessed by an IRC. | |
| End point type | Secondary |
| End point timeframe: Up to approximately 9 years | |

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|-----------------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 347 | 335 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 50 | 59 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Pain Progression

| | |
|-----------------|--------------------------|
| End point title | Time to Pain Progression |
|-----------------|--------------------------|

End point description:

Time to pain progression was assessed as the time from randomization to the date of initial progression classification. Pain progression was defined as the occurrence of 1 of the following and confirmed by 2 consecutive evaluations (To qualify as progression, the participant must have a BPI-SF worst pain score > 4 during pain progression): 1) a ≥ 2 point and 30% increase from Baseline in BPI-SF worst pain score without an increase in analgesic use, or 2) a 25% or more increase in analgesic use from Baseline without a decrease in BPI-SF worst pain score from Baseline. Brief Pain Inventory - Short Form (m-BPI-SF) is a participant rated 11-point Likert rating scale ranged from 0 (no pain) to 10 (worst pain imaginable). ITT population included all participants who were randomized. 99999 indicates that Median, upper limit and/or lower limit of CI was not estimable due to insufficient number of participants with events.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to approximately 9 years

| End point values | Placebo + LenDex | Ixazomib + LenDex | | |
|----------------------------------|-----------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 354 | 351 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 47.1 (30.88 to 99999) | 99999 (57.59 to 99999) | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Time to Pain Progression

| | |
|-------------------|--------------------------------------|
| Comparison groups | Placebo + LenDex v Ixazomib + LenDex |
|-------------------|--------------------------------------|

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 705 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[20] |
| P-value | = 0.26 ^[21] |
| Method | Log Rank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.661 |
| upper limit | 1.12 |

Notes:

[20] - Hazard ratio is based on an unadjusted Cox's proportional hazard regression model stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

[21] - Log-rank test is stratified by age (<75 years vs ≥75), ISS (stage I or II vs stage III), and BPI-SF worst pain score (<4 vs ≥4) at screening.

Secondary: Cmax: Maximum Plasma Concentration for Ixazomib

| | |
|---|---|
| End point title | Cmax: Maximum Plasma Concentration for Ixazomib |
| End point description: | |
| Pharmacokinetic (PK) analysis population is defined as subjects with at least one PK sample that was collected and analyzed. 'N' indicates overall number of participants available for analyses. 'n' indicates number of participants available for analysis at the given timepoint. | |
| End point type | Secondary |
| End point timeframe: | |
| Cycle 1 Day 1: Post-dose at multiple timepoints up to 4 hours; Pre-dose at Cycle 1 Day 14, Cycles 2-3 Day 1 and Day 14, Cycles 4-11 Day 1 (Each cycle length = 28 days) | |

| End point values | Ixazomib | | | |
|---|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 331 | | | |
| Units: millilitre(s) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1: 1 Hour Post-dose (n= 331) | 44.745 (± 35.9404) | | | |
| Cycle 1 Day 1: 4 Hours Post-dose (n= 320) | 16.253 (± 17.0407) | | | |
| Cycle 1 Day 14: Pre-dose (n= 327) | 7.867 (± 15.4420) | | | |
| Cycle 2 Day 1: Pre-dose (n= 320) | 2.664 (± 2.2770) | | | |
| Cycle 2 Day 14: Pre-dose (n= 302) | 8.521 (± 14.7411) | | | |
| Cycle 3 Day 1: Pre-dose (n= 300) | 2.763 (± 1.6318) | | | |
| Cycle 3 Day 14: Pre-dose (n= 275) | 8.490 (± 17.6720) | | | |
| Cycle 4 Day 1: Pre-dose (n= 284) | 3.284 (± 6.1116) | | | |
| Cycle 5 Day 1: Pre-dose (n= 270) | 3.594 (± 13.2046) | | | |

| | | | | |
|-----------------------------------|------------------|--|--|--|
| Cycle 6 Day 1: Pre-dose (n= 260) | 2.603 (± 1.5242) | | | |
| Cycle 7 Day 1: Pre-dose (n= 258) | 2.598 (± 1.4658) | | | |
| Cycle 8 Day 1: Pre-dose (n= 251) | 2.539 (± 1.5549) | | | |
| Cycle 9 Day 1: Pre-dose (n= 242) | 2.593 (± 2.0867) | | | |
| Cycle 10 Day 1: Pre-dose (n= 238) | 2.536 (± 1.7431) | | | |
| Cycle 11 Day 1: Pre-dose (n=224) | 2.667 (± 4.5448) | | | |
| Cycle 12 Day 1: Pre-dose (n=217) | 2.686 (± 1.8949) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With New or Worsening of Existing Skeletal-related Events (SREs)

| | |
|-----------------|---|
| End point title | Percentage of Participants With New or Worsening of Existing Skeletal-related Events (SREs) |
|-----------------|---|

End point description:

SRE is defined as new fractures [including vertebral compression fractures], irradiation of or surgery on bone, or spinal cord compression. Safety population is defined as all participants who receive at least 1 dose of any study drug. Data for safety is summarized as per the duration of exposure to study treatment (exposure up to 18 cycles; exposure ≥19 cycles).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of randomization through 30 days after the last dose of study drug up to end of study (up to approximately 9 years)

| End point values | Placebo + LenDex (Exposure Up to 18 Cycles) | Ixazomib+ LenDex (Exposure Up to 18 Cycles) | Placebo + LenDex (Exposure ≥19 Cycles) | Ixazomib + LenDex (Exposure ≥19 Cycles) |
|-----------------------------------|--|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 160 | 163 | 189 | 191 |
| Units: percentage of participants | | | | |
| number (not applicable) | 14 | 10 | 28 | 25 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of randomization through 30 days after the last dose of study drug up to end of study (approximately 9 years)

Adverse event reporting additional description:

Safety population. 4 participants randomized to placebo received ixazomib during study and were included in ixazomib arm for safety population. 1 participant randomized to each arm withdrew from study and was not included. Data for safety is summarized per the duration of exposure to study treatment (exposure up to 18 cycles; exposure ≥ 19 cycles).

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 25 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Placebo + LenDex (Exposure Up to 18 Cycles) |
|-----------------------|---|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | Placebo + LenDex (Exposure ≥ 19 Cycles) |
|-----------------------|--|

Reporting group description:

Participants who were randomly assigned to receive Placebo were administered ixazomib 4.0 mg placebo matching capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) up to 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib placebo matching capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months).

| | |
|-----------------------|---|
| Reporting group title | Ixazomib + LenDex (Exposure ≥ 19 Cycles) |
|-----------------------|---|

Reporting group description:

Participants who were randomly assigned to receive Ixazomib were administered ixazomib 4.0 mg placebo matching capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) up to 18 cycles (each cycle was of 28 days). Following Cycle 18, participants received 3.0 mg ixazomib capsule as single oral dose on Days 1, 8 and 15 along with lenalidomide 10 mg capsules orally on Days 1-21 in each 28-day cycle until progressive disease or unacceptable toxicity, whichever comes first up to end of study (up to approximately 109 months).

| | |
|-----------------------|---|
| Reporting group title | Ixazomib+ LenDex (Exposure Up to 18 Cycles) |
|-----------------------|---|

Reporting group description:

Participants who were randomly assigned to receive Ixazomib were administered ixazomib 4.0 mg capsule single oral dose on Days 1, 8 and 15 along with standard regimen of LenDex (lenalidomide 25 mg capsules orally on Days 1-21 and dexamethasone 40 mg tablets orally on Days 1, 8, 15 and 22) up to 18 cycles (each cycle was of 28 days).

| Serious adverse events | Placebo + LenDex (Exposure Up to 18 Cycles) | Placebo + LenDex (Exposure ≥ 19 Cycles) | Ixazomib + LenDex (Exposure ≥ 19 Cycles) |
|--|---|--|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 105 / 160 (65.63%) | 119 / 189 (62.96%) | 125 / 191 (65.45%) |
| number of deaths (all causes) | 107 | 63 | 63 |
| number of deaths resulting from adverse events | 17 | 5 | 7 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|-----------------|-----------------|------------------|
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute erythroid leukaemia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 6 / 189 (3.17%) | 12 / 191 (6.28%) |
| occurrences causally related to treatment / all | 0 / 1 | 6 / 6 | 8 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bowen's disease | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma pancreas | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder adenocarcinoma | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal adenoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric cancer | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to liver | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung carcinoma cell type unspecified stage I | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large granular lymphocytosis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sarcomatoid carcinoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 4 / 191 (2.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Plasma cell myeloma | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Plasma cell leukaemia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer recurrent | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transitional cell cancer of the renal pelvis and ureter | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Superficial spreading melanoma stage unspecified | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 4 / 189 (2.12%) | 5 / 191 (2.62%) |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 4 | 5 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Peripheral artery stenosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral arterial occlusive disease | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic stenosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 5 / 189 (2.65%) | 4 / 191 (2.09%) |
| occurrences causally related to treatment / all | 3 / 3 | 5 / 5 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 2 / 189 (1.06%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Phlebitis | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 5 / 160 (3.13%) | 2 / 189 (1.06%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 4 / 8 | 1 / 3 | 1 / 4 |
| deaths causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| Complication associated with device | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest pain | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperthermia | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incarcerated hernia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 3 / 189 (1.59%) | 4 / 191 (2.09%) |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 4 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stent-graft endoleak | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 3 |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Testicular oedema | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystocele | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 0 / 189 (0.00%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 7 / 160 (4.38%) | 5 / 189 (2.65%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 7 / 7 | 6 / 6 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis aspiration | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paranasal cyst | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infiltration | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 5 / 189 (2.65%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 6 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Delirium | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hallucination | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obsessive thoughts | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Device breakage | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device loosening | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blast cells present | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcus test positive | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 2 / 189 (1.06%) | 4 / 191 (2.09%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 2 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fracture displacement | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ankle fracture | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic injury | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical vertebral fracture | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis radiation | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 3 / 189 (1.59%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 4 / 189 (2.12%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radius fracture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb traumatic amputation | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar vertebral fracture | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary retention postoperative | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulna fracture | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 2 / 189 (1.06%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute coronary syndrome | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 3 / 189 (1.59%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 3 / 189 (1.59%) | 4 / 191 (2.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 2 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive heart disease | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 5 / 160 (3.13%) | 2 / 189 (1.06%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 3 / 6 | 1 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiomyopathy | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Ischaemic cardiomyopathy | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prosthetic cardiac valve malfunction | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Demyelinating polyneuropathy | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervicobrachial syndrome | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 1 / 189 (0.53%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cerebral infarction | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haematoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Intraventricular haemorrhage | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxic-ischaemic encephalopathy | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperaesthesia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Hemiplegia | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lacunar infarction | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Senile dementia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peroneal nerve palsy | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Posterior reversible encephalopathy syndrome | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorder | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal claudication | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 5 / 189 (2.65%) | 4 / 191 (2.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 5 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thalamic infarction | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thalamus haemorrhage | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 2 / 189 (1.06%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 2 / 189 (1.06%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Heparin-induced thrombocytopenia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Angle closure glaucoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amaurosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cataract | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 3 / 189 (1.59%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eyelid ptosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Optic nerve sheath haemorrhage | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal adhesions | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal wall haematoma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal hernia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 7 / 191 (3.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 6 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticular perforation | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal ulcer | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric volvulus | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis haemorrhagic | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal ischaemia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal perforation | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periodontal disease | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retroperitoneal haemorrhage | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 4 / 191 (2.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal prolapse | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Umbilical hernia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Volvulus | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis acute | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug eruption | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug reaction with eosinophilia and systemic symptoms | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stevens-Johnson syndrome | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic epidermal necrolysis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic skin eruption | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 8 / 160 (5.00%) | 2 / 189 (1.06%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 2 / 9 | 0 / 2 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Focal segmental glomerulosclerosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myeloma cast nephropathy | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephritis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 160 (1.88%) | 0 / 189 (0.00%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 2 / 189 (1.06%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone lesion | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone pain | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chondrocalcinosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chondrocalcinosis pyrophosphate | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mobility decreased | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Kyphosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemarthrosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fracture pain | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Crystal arthropathy | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 4 / 189 (2.12%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sarcopenia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 2 / 189 (1.06%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteolysis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoporotic fracture | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 160 (1.25%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Synovitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal stenosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bartholinitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 5 / 189 (2.65%) | 4 / 191 (2.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess jaw | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis bacterial | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 2 / 189 (1.06%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bursitis infective | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis staphylococcal | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 3 / 189 (1.59%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 3 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis E | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 2 / 189 (1.06%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fungal oesophagitis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia sepsis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 2 / 189 (1.06%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis | | | |

| | | | |
|---|-------------------|------------------|-------------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural infection | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 16 / 160 (10.00%) | 13 / 189 (6.88%) | 22 / 191 (11.52%) |
| occurrences causally related to treatment / all | 7 / 18 | 7 / 13 | 15 / 26 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia parainfluenzae viral | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia legionella | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia influenzal | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia haemophilus | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 2 / 191 (1.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatitis Escherichia coli | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 4 / 189 (2.12%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 3 / 4 | 2 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Sepsis syndrome | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Soft tissue infection | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis aspergillus | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 2 / 6 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 0 |
| Superinfection bacterial | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic shock syndrome staphylococcal | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 3 / 189 (1.59%) | 6 / 191 (3.14%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 4 | 1 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral uveitis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 5 / 191 (2.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 5 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypervolaemia | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 1 / 189 (0.53%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 160 (1.25%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 4 / 191 (2.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 2 / 189 (1.06%) | 3 / 191 (1.57%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 2 / 189 (1.06%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 1 / 191 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 189 (0.00%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 189 (0.53%) | 0 / 191 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|-------------------------------|--|--|--|
| Serious adverse events | Ixazomib+ LenDex (Exposure Up to 18 Cycles) | | |
|-------------------------------|--|--|--|

| | | | |
|---|--------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 119 / 163 (73.01%) | | |
| number of deaths (all causes) | 95 | | |
| number of deaths resulting from adverse events | 21 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute erythroid leukaemia | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bowen's disease | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Adenocarcinoma pancreas | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gallbladder adenocarcinoma | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colorectal adenoma | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colorectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chronic myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric cancer | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metastases to liver | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung neoplasm malignant | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung carcinoma cell type unspecified stage I | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large granular lymphocytosis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastatic malignant melanoma | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatic carcinoma | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Papillary thyroid cancer | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sarcomatoid carcinoma | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Squamous cell carcinoma | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Prostate cancer | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 3 | | |
| Plasma cell leukaemia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate cancer recurrent | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transitional cell cancer of the renal pelvis and ureter | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Superficial spreading melanoma stage unspecified | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |

| | | | | |
|---|-----------------|--|--|--|
| Peripheral artery stenosis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral arterial occlusive disease | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Orthostatic hypotension | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aortic stenosis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Deep vein thrombosis | | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Embolism | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypotension | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypovolaemic shock | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral ischaemia | | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Phlebitis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences causally related to treatment / all | 1 / 6 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Complication associated with device | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Death | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Fatigue | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chest pain | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Generalised oedema | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hyperthermia | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Incarcerated hernia | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Inflammation | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pain | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Malaise | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Multiple organ dysfunction syndrome | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stent-graft endoleak | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Testicular oedema | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cystocele | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences causally related to treatment / all | 1 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chronic obstructive pulmonary disease | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 2 / 163 (1.23%) | | | |
| occurrences causally related to treatment / all | 2 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypoxia | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute respiratory failure | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Acute respiratory distress syndrome | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute pulmonary oedema | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Asthma | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary embolism | | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | | |
| occurrences causally related to treatment / all | 3 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonitis aspiration | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonitis | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Paranasal cyst | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Delirium | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Depression | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hallucination | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Obsessive thoughts | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Product issues | | | |
| Device breakage | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device loosening | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |

| | | | |
|---|-----------------|--|--|
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blast cells present | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Staphylococcus test positive | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|-----------------|--|--|--|
| Hip fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fracture displacement | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Humerus fracture | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ankle fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aortic injury | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cervical vertebral fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cystitis radiation | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fall | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Femoral neck fracture | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Femur fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Radius fracture | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post procedural haemorrhage | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pelvic fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Overdose | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin laceration | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower limb fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Limb traumatic amputation | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint dislocation | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lumbar vertebral fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary retention postoperative | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper limb fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ulna fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thoracic vertebral fracture | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Subdural haematoma | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal compression fracture | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Angina unstable | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac arrest | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 4 / 163 (2.45%) | | | |
| occurrences causally related to treatment / all | 1 / 4 | | | |
| deaths causally related to treatment / all | 1 / 4 | | | |
| Hypertensive heart disease | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure congestive | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardio-respiratory arrest | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiomyopathy | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Coronary artery disease | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure | | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | | |
| occurrences causally related to treatment / all | 2 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ischaemic cardiomyopathy | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Myocardial infarction | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prosthetic cardiac valve malfunction | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Demyelinating polyneuropathy | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cervicobrachial syndrome | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haematoma | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Embolic stroke | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intraventricular haemorrhage | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypoxic-ischaemic encephalopathy | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hyperaesthesia | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic encephalopathy | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hemiplegia | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhage intracranial | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epilepsy | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Seizure | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lacunar infarction | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lethargy | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Loss of consciousness | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Senile dementia | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral sensory neuropathy | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peroneal nerve palsy | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Posterior reversible encephalopathy syndrome | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Presyncope | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nervous system disorder | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal claudication | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences causally related to treatment / all | 2 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thalamic infarction | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thalamus haemorrhage | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences causally related to treatment / all | 5 / 7 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences causally related to treatment / all | 3 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Heparin-induced thrombocytopenia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences causally related to treatment / all | 2 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Angle closure glaucoma | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Amaurosis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eyelid ptosis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Optic nerve sheath haemorrhage | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |

| | | | | |
|---|-----------------|--|--|--|
| Abdominal adhesions | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dental caries | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain upper | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal wall haematoma | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Constipation | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal hernia | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 8 / 163 (4.91%) | | | |
| occurrences causally related to treatment / all | 7 / 10 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticular perforation | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Duodenal ulcer | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Faecaloma | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric volvulus | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enterocolitis haemorrhagic | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Inguinal hernia | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal ischaemia | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal perforation | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Pancreatitis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophagitis | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Periodontal disease | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Retroperitoneal haemorrhage | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal haemorrhage | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal prolapse | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Umbilical hernia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Volvulus | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis acute | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug eruption | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Drug reaction with eosinophilia and systemic symptoms | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Stevens-Johnson syndrome | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash erythematous | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash macular | | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash maculo-papular | | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | | |
| occurrences causally related to treatment / all | 4 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash papular | | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Toxic epidermal necrolysis | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Toxic skin eruption | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences causally related to treatment / all | 2 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Focal segmental glomerulosclerosis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myeloma cast nephropathy | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nephritis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bone lesion | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bone pain | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 2 / 163 (1.23%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chondrocalcinosis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chondrocalcinosis pyrophosphate | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mobility decreased | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Kyphosis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intervertebral disc protrusion | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemarthrosis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fracture pain | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Crystal arthropathy | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pathological fracture | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences causally related to treatment / all | 1 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sarcopenia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteolysis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteoporotic fracture | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Synovitis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal stenosis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atypical pneumonia | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bartholinitis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchitis | | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | | |
| occurrences causally related to treatment / all | 2 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abscess jaw | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device related infection | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cystitis bacterial | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile infection | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile colitis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchopulmonary aspergillosis | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Campylobacter gastroenteritis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bursitis infective | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis staphylococcal | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis E | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 4 / 163 (2.45%) | | | |
| occurrences causally related to treatment / all | 2 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fungal oesophagitis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia sepsis | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Erysipelas | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endocarditis | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonitis | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Parainfluenzae virus infection | | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Meningitis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleural infection | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 22 / 163 (13.50%) | | |
| occurrences causally related to treatment / all | 11 / 28 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Lower respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia parainfluenzae viral | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia legionella | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia influenzal | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia haemophilus | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pseudomonal sepsis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostatitis Escherichia coli | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences causally related to treatment / all | 3 / 4 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Sepsis syndrome | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Soft tissue infection | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin infection | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinusitis aspergillus | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Septic shock | | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | | |
| occurrences causally related to treatment / all | 1 / 5 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Superinfection bacterial | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tonsillitis | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tooth infection | | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Toxic shock syndrome staphylococcal | | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper respiratory tract infection | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences causally related to treatment / all | 3 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral uveitis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypervolaemia | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Failure to thrive | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences causally related to treatment / all | 4 / 9 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malnutrition | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Placebo + LenDex (Exposure Up to 18 Cycles) | Placebo + LenDex (Exposure ≥19 Cycles) | Ixazomib + LenDex (Exposure ≥19 Cycles) |
|---|---|--|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 159 / 160 (99.38%) | 189 / 189 (100.00%) | 191 / 191 (100.00%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 9 / 160 (5.63%) | 18 / 189 (9.52%) | 29 / 191 (15.18%) |
| occurrences (all) | 10 | 20 | 32 |
| Hypotension | | | |
| subjects affected / exposed | 12 / 160 (7.50%) | 11 / 189 (5.82%) | 15 / 191 (7.85%) |
| occurrences (all) | 12 | 12 | 20 |
| Haematoma | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 7 / 189 (3.70%) | 10 / 191 (5.24%) |
| occurrences (all) | 1 | 9 | 12 |
| Flushing | | | |
| subjects affected / exposed | 5 / 160 (3.13%) | 12 / 189 (6.35%) | 6 / 191 (3.14%) |
| occurrences (all) | 5 | 15 | 6 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 15 / 160 (9.38%) | 13 / 189 (6.88%) | 4 / 191 (2.09%) |
| occurrences (all) | 16 | 14 | 4 |
| Hot flush | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 14 / 189 (7.41%) | 4 / 191 (2.09%) |
| occurrences (all) | 2 | 15 | 4 |
| General disorders and administration site conditions | | | |

| | | | |
|---|-------------------|-------------------|--------------------|
| Pyrexia | | | |
| subjects affected / exposed | 20 / 160 (12.50%) | 29 / 189 (15.34%) | 33 / 191 (17.28%) |
| occurrences (all) | 22 | 43 | 45 |
| Peripheral swelling | | | |
| subjects affected / exposed | 8 / 160 (5.00%) | 12 / 189 (6.35%) | 17 / 191 (8.90%) |
| occurrences (all) | 12 | 14 | 23 |
| Oedema peripheral | | | |
| subjects affected / exposed | 52 / 160 (32.50%) | 64 / 189 (33.86%) | 106 / 191 (55.50%) |
| occurrences (all) | 71 | 103 | 170 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 10 / 189 (5.29%) | 14 / 191 (7.33%) |
| occurrences (all) | 2 | 11 | 17 |
| Malaise | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 16 / 189 (8.47%) | 17 / 191 (8.90%) |
| occurrences (all) | 4 | 18 | 18 |
| Influenza like illness | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 11 / 189 (5.82%) | 16 / 191 (8.38%) |
| occurrences (all) | 4 | 13 | 23 |
| Fatigue | | | |
| subjects affected / exposed | 53 / 160 (33.13%) | 52 / 189 (27.51%) | 69 / 191 (36.13%) |
| occurrences (all) | 71 | 80 | 115 |
| Chills | | | |
| subjects affected / exposed | 10 / 160 (6.25%) | 7 / 189 (3.70%) | 12 / 191 (6.28%) |
| occurrences (all) | 12 | 7 | 15 |
| Asthenia | | | |
| subjects affected / exposed | 44 / 160 (27.50%) | 53 / 189 (28.04%) | 58 / 191 (30.37%) |
| occurrences (all) | 56 | 76 | 84 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 6 / 160 (3.75%) | 7 / 189 (3.70%) | 15 / 191 (7.85%) |
| occurrences (all) | 6 | 7 | 17 |
| Productive cough | | | |
| subjects affected / exposed | 8 / 160 (5.00%) | 5 / 189 (2.65%) | 12 / 191 (6.28%) |
| occurrences (all) | 8 | 7 | 13 |
| Oropharyngeal pain | | | |

| | | | |
|-----------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed | 4 / 160 (2.50%) | 12 / 189 (6.35%) | 12 / 191 (6.28%) |
| occurrences (all) | 5 | 12 | 19 |
| Hiccups | | | |
| subjects affected / exposed | 6 / 160 (3.75%) | 10 / 189 (5.29%) | 5 / 191 (2.62%) |
| occurrences (all) | 10 | 19 | 6 |
| Epistaxis | | | |
| subjects affected / exposed | 11 / 160 (6.88%) | 16 / 189 (8.47%) | 12 / 191 (6.28%) |
| occurrences (all) | 13 | 20 | 14 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 7 / 160 (4.38%) | 14 / 189 (7.41%) | 12 / 191 (6.28%) |
| occurrences (all) | 7 | 16 | 15 |
| Dyspnoea | | | |
| subjects affected / exposed | 32 / 160 (20.00%) | 26 / 189 (13.76%) | 39 / 191 (20.42%) |
| occurrences (all) | 39 | 36 | 64 |
| Dysphonia | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 12 / 189 (6.35%) | 4 / 191 (2.09%) |
| occurrences (all) | 4 | 16 | 4 |
| Cough | | | |
| subjects affected / exposed | 24 / 160 (15.00%) | 37 / 189 (19.58%) | 53 / 191 (27.75%) |
| occurrences (all) | 26 | 50 | 85 |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 10 / 189 (5.29%) | 11 / 191 (5.76%) |
| occurrences (all) | 3 | 11 | 13 |
| Anxiety | | | |
| subjects affected / exposed | 15 / 160 (9.38%) | 25 / 189 (13.23%) | 26 / 191 (13.61%) |
| occurrences (all) | 17 | 35 | 32 |
| Confusional state | | | |
| subjects affected / exposed | 15 / 160 (9.38%) | 11 / 189 (5.82%) | 11 / 191 (5.76%) |
| occurrences (all) | 18 | 13 | 11 |
| Irritability | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 11 / 189 (5.82%) | 4 / 191 (2.09%) |
| occurrences (all) | 3 | 13 | 4 |
| Insomnia | | | |
| subjects affected / exposed | 27 / 160 (16.88%) | 68 / 189 (35.98%) | 70 / 191 (36.65%) |
| occurrences (all) | 33 | 85 | 84 |

| | | | |
|--|-------------------------|-------------------------|-------------------------|
| Depression subjects affected / exposed occurrences (all) | 10 / 160 (6.25%) 10 | 14 / 189 (7.41%) 15 | 26 / 191 (13.61%) 29 |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 160 (0.63%) 1 | 4 / 189 (2.12%) 5 | 10 / 191 (5.24%) 12 |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 8 / 160 (5.00%) 9 | 12 / 189 (6.35%) 18 | 16 / 191 (8.38%) 18 |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 11 / 160 (6.88%) 17 | 13 / 189 (6.88%) 45 | 18 / 191 (9.42%) 47 |
| Platelet count decreased subjects affected / exposed occurrences (all) | 6 / 160 (3.75%) 13 | 4 / 189 (2.12%) 4 | 15 / 191 (7.85%) 40 |
| Weight decreased subjects affected / exposed occurrences (all) | 20 / 160 (12.50%) 24 | 30 / 189 (15.87%) 40 | 35 / 191 (18.32%) 51 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 7 / 160 (4.38%) 7 | 20 / 189 (10.58%) 25 | 19 / 191 (9.95%) 23 |
| Fall subjects affected / exposed occurrences (all) | 9 / 160 (5.63%) 10 | 35 / 189 (18.52%) 67 | 45 / 191 (23.56%) 68 |
| Procedural pain subjects affected / exposed occurrences (all) | 2 / 160 (1.25%) 2 | 11 / 189 (5.82%) 11 | 6 / 191 (3.14%) 6 |
| Skin laceration subjects affected / exposed occurrences (all) | 4 / 160 (2.50%) 5 | 10 / 189 (5.29%) 10 | 8 / 191 (4.19%) 10 |
| Cardiac disorders | | | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 8 / 160 (5.00%) 9 | 11 / 189 (5.82%) 12 | 7 / 191 (3.66%) 7 |

| | | | |
|---|-------------------------|-------------------------|--------------------------|
| Cardiac failure subjects affected / exposed occurrences (all) | 3 / 160 (1.88%) 3 | 2 / 189 (1.06%) 2 | 1 / 191 (0.52%) 1 |
| Palpitations subjects affected / exposed occurrences (all) | 1 / 160 (0.63%) 1 | 8 / 189 (4.23%) 8 | 11 / 191 (5.76%) 13 |
| Nervous system disorders | | | |
| Tremor subjects affected / exposed occurrences (all) | 23 / 160 (14.38%) 27 | 27 / 189 (14.29%) 39 | 19 / 191 (9.95%) 20 |
| Syncope subjects affected / exposed occurrences (all) | 2 / 160 (1.25%) 2 | 6 / 189 (3.17%) 8 | 14 / 191 (7.33%) 20 |
| Sciatica subjects affected / exposed occurrences (all) | 3 / 160 (1.88%) 3 | 11 / 189 (5.82%) 12 | 16 / 191 (8.38%) 18 |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 27 / 160 (16.88%) 29 | 57 / 189 (30.16%) 93 | 85 / 191 (44.50%) 152 |
| Paraesthesia subjects affected / exposed occurrences (all) | 13 / 160 (8.13%) 14 | 21 / 189 (11.11%) 33 | 25 / 191 (13.09%) 34 |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 3 / 160 (1.88%) 3 | 9 / 189 (4.76%) 11 | 14 / 191 (7.33%) 16 |
| Memory impairment subjects affected / exposed occurrences (all) | 3 / 160 (1.88%) 3 | 10 / 189 (5.29%) 10 | 7 / 191 (3.66%) 11 |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 7 / 160 (4.38%) 7 | 11 / 189 (5.82%) 16 | 14 / 191 (7.33%) 17 |
| Headache subjects affected / exposed occurrences (all) | 22 / 160 (13.75%) 25 | 36 / 189 (19.05%) 50 | 33 / 191 (17.28%) 46 |
| Dysgeusia | | | |

| | | | |
|--|-------------------------|--------------------------|--------------------------|
| subjects affected / exposed occurrences (all) | 14 / 160 (8.75%) 15 | 12 / 189 (6.35%) 13 | 32 / 191 (16.75%) 35 |
| Dizziness subjects affected / exposed occurrences (all) | 31 / 160 (19.38%) 38 | 36 / 189 (19.05%) 75 | 31 / 191 (16.23%) 42 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 56 / 160 (35.00%) 92 | 51 / 189 (26.98%) 85 | 58 / 191 (30.37%) 107 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 15 / 160 (9.38%) 30 | 14 / 189 (7.41%) 25 | 24 / 191 (12.57%) 41 |
| Neutropenia subjects affected / exposed occurrences (all) | 36 / 160 (22.50%) 92 | 48 / 189 (25.40%) 135 | 39 / 191 (20.42%) 99 |
| Ear and labyrinth disorders | | | |
| Hypoacusis subjects affected / exposed occurrences (all) | 0 / 160 (0.00%) 0 | 6 / 189 (3.17%) 7 | 10 / 191 (5.24%) 11 |
| Vertigo subjects affected / exposed occurrences (all) | 4 / 160 (2.50%) 4 | 18 / 189 (9.52%) 21 | 22 / 191 (11.52%) 26 |
| Eye disorders | | | |
| Cataract subjects affected / exposed occurrences (all) | 6 / 160 (3.75%) 7 | 41 / 189 (21.69%) 55 | 54 / 191 (28.27%) 74 |
| Dry eye subjects affected / exposed occurrences (all) | 1 / 160 (0.63%) 1 | 6 / 189 (3.17%) 7 | 17 / 191 (8.90%) 19 |
| Vision blurred subjects affected / exposed occurrences (all) | 6 / 160 (3.75%) 6 | 22 / 189 (11.64%) 22 | 25 / 191 (13.09%) 26 |
| Gastrointestinal disorders | | | |
| Abdominal distension subjects affected / exposed occurrences (all) | 6 / 160 (3.75%) 6 | 11 / 189 (5.82%) 14 | 11 / 191 (5.76%) 14 |
| Abdominal pain | | | |

| | | | |
|----------------------------------|-------------------|--------------------|--------------------|
| subjects affected / exposed | 10 / 160 (6.25%) | 38 / 189 (20.11%) | 30 / 191 (15.71%) |
| occurrences (all) | 15 | 48 | 44 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 13 / 160 (8.13%) | 29 / 189 (15.34%) | 23 / 191 (12.04%) |
| occurrences (all) | 13 | 39 | 27 |
| Constipation | | | |
| subjects affected / exposed | 61 / 160 (38.13%) | 82 / 189 (43.39%) | 92 / 191 (48.17%) |
| occurrences (all) | 78 | 128 | 120 |
| Dental caries | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 11 / 189 (5.82%) | 6 / 191 (3.14%) |
| occurrences (all) | 2 | 15 | 8 |
| Diarrhoea | | | |
| subjects affected / exposed | 48 / 160 (30.00%) | 115 / 189 (60.85%) | 147 / 191 (76.96%) |
| occurrences (all) | 82 | 292 | 378 |
| Nausea | | | |
| subjects affected / exposed | 35 / 160 (21.88%) | 63 / 189 (33.33%) | 78 / 191 (40.84%) |
| occurrences (all) | 49 | 100 | 128 |
| Dyspepsia | | | |
| subjects affected / exposed | 16 / 160 (10.00%) | 22 / 189 (11.64%) | 21 / 191 (10.99%) |
| occurrences (all) | 17 | 34 | 29 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 10 / 189 (5.29%) | 13 / 191 (6.81%) |
| occurrences (all) | 3 | 13 | 15 |
| Haemorrhoids | | | |
| subjects affected / exposed | 6 / 160 (3.75%) | 15 / 189 (7.94%) | 12 / 191 (6.28%) |
| occurrences (all) | 7 | 16 | 13 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 10 / 189 (5.29%) | 5 / 191 (2.62%) |
| occurrences (all) | 0 | 13 | 5 |
| Dry mouth | | | |
| subjects affected / exposed | 14 / 160 (8.75%) | 12 / 189 (6.35%) | 13 / 191 (6.81%) |
| occurrences (all) | 15 | 14 | 16 |
| Toothache | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 15 / 189 (7.94%) | 8 / 191 (4.19%) |
| occurrences (all) | 4 | 16 | 11 |
| Stomatitis | | | |

| | | | |
|--|-------------------|-------------------|-------------------|
| subjects affected / exposed | 9 / 160 (5.63%) | 8 / 189 (4.23%) | 15 / 191 (7.85%) |
| occurrences (all) | 9 | 9 | 21 |
| Vomiting | | | |
| subjects affected / exposed | 13 / 160 (8.13%) | 33 / 189 (17.46%) | 66 / 191 (34.55%) |
| occurrences (all) | 23 | 53 | 170 |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 8 / 160 (5.00%) | 22 / 189 (11.64%) | 31 / 191 (16.23%) |
| occurrences (all) | 8 | 26 | 35 |
| Alopecia | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 8 / 189 (4.23%) | 13 / 191 (6.81%) |
| occurrences (all) | 3 | 8 | 14 |
| Urticaria | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 5 / 189 (2.65%) | 10 / 191 (5.24%) |
| occurrences (all) | 3 | 6 | 12 |
| Rash papular | | | |
| subjects affected / exposed | 8 / 160 (5.00%) | 4 / 189 (2.12%) | 12 / 191 (6.28%) |
| occurrences (all) | 8 | 5 | 13 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 18 / 160 (11.25%) | 22 / 189 (11.64%) | 43 / 191 (22.51%) |
| occurrences (all) | 35 | 40 | 111 |
| Rash macular | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 11 / 189 (5.82%) | 27 / 191 (14.14%) |
| occurrences (all) | 7 | 14 | 39 |
| Rash erythematous | | | |
| subjects affected / exposed | 10 / 160 (6.25%) | 3 / 189 (1.59%) | 18 / 191 (9.42%) |
| occurrences (all) | 12 | 3 | 32 |
| Rash | | | |
| subjects affected / exposed | 9 / 160 (5.63%) | 7 / 189 (3.70%) | 18 / 191 (9.42%) |
| occurrences (all) | 12 | 7 | 25 |
| Pruritus | | | |
| subjects affected / exposed | 13 / 160 (8.13%) | 29 / 189 (15.34%) | 37 / 191 (19.37%) |
| occurrences (all) | 15 | 42 | 59 |
| Night sweats | | | |
| subjects affected / exposed | 9 / 160 (5.63%) | 9 / 189 (4.76%) | 5 / 191 (2.62%) |
| occurrences (all) | 9 | 11 | 6 |

| | | | |
|---|-------------------|-------------------|-------------------|
| Erythema | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 20 / 189 (10.58%) | 16 / 191 (8.38%) |
| occurrences (all) | 2 | 21 | 21 |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 29 / 160 (18.13%) | 50 / 189 (26.46%) | 50 / 191 (26.18%) |
| occurrences (all) | 34 | 78 | 73 |
| Osteoarthritis | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 13 / 189 (6.88%) | 24 / 191 (12.57%) |
| occurrences (all) | 4 | 16 | 25 |
| Neck pain | | | |
| subjects affected / exposed | 9 / 160 (5.63%) | 25 / 189 (13.23%) | 22 / 191 (11.52%) |
| occurrences (all) | 9 | 26 | 25 |
| Myalgia | | | |
| subjects affected / exposed | 9 / 160 (5.63%) | 24 / 189 (12.70%) | 33 / 191 (17.28%) |
| occurrences (all) | 13 | 32 | 40 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 14 / 189 (7.41%) | 13 / 191 (6.81%) |
| occurrences (all) | 0 | 19 | 15 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 12 / 160 (7.50%) | 27 / 189 (14.29%) | 25 / 191 (13.09%) |
| occurrences (all) | 14 | 33 | 31 |
| Muscle spasms | | | |
| subjects affected / exposed | 27 / 160 (16.88%) | 50 / 189 (26.46%) | 52 / 191 (27.23%) |
| occurrences (all) | 38 | 82 | 96 |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 11 / 189 (5.82%) | 12 / 191 (6.28%) |
| occurrences (all) | 1 | 12 | 14 |
| Bone pain | | | |
| subjects affected / exposed | 10 / 160 (6.25%) | 24 / 189 (12.70%) | 20 / 191 (10.47%) |
| occurrences (all) | 10 | 30 | 24 |
| Back pain | | | |
| subjects affected / exposed | 34 / 160 (21.25%) | 67 / 189 (35.45%) | 64 / 191 (33.51%) |
| occurrences (all) | 36 | 101 | 90 |
| Arthritis | | | |

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|-----------------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 160 (0.00%) | 4 / 189 (2.12%) | 16 / 191 (8.38%) |
| occurrences (all) | 0 | 5 | 17 |
| Arthralgia | | | |
| subjects affected / exposed | 23 / 160 (14.38%) | 81 / 189 (42.86%) | 76 / 191 (39.79%) |
| occurrences (all) | 34 | 155 | 143 |
| Muscular weakness | | | |
| subjects affected / exposed | 12 / 160 (7.50%) | 19 / 189 (10.05%) | 18 / 191 (9.42%) |
| occurrences (all) | 13 | 22 | 25 |
| Pathological fracture | | | |
| subjects affected / exposed | 5 / 160 (3.13%) | 20 / 189 (10.58%) | 10 / 191 (5.24%) |
| occurrences (all) | 7 | 23 | 11 |
| Pain in jaw | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 8 / 189 (4.23%) | 10 / 191 (5.24%) |
| occurrences (all) | 3 | 10 | 11 |
| Infections and infestations | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 5 / 189 (2.65%) | 18 / 191 (9.42%) |
| occurrences (all) | 2 | 9 | 20 |
| Cellulitis | | | |
| subjects affected / exposed | 5 / 160 (3.13%) | 3 / 189 (1.59%) | 11 / 191 (5.76%) |
| occurrences (all) | 5 | 3 | 15 |
| Bronchitis | | | |
| subjects affected / exposed | 13 / 160 (8.13%) | 51 / 189 (26.98%) | 74 / 191 (38.74%) |
| occurrences (all) | 15 | 109 | 168 |
| Cystitis | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 12 / 189 (6.35%) | 13 / 191 (6.81%) |
| occurrences (all) | 2 | 20 | 19 |
| Urinary tract infection | | | |
| subjects affected / exposed | 14 / 160 (8.75%) | 27 / 189 (14.29%) | 30 / 191 (15.71%) |
| occurrences (all) | 18 | 44 | 56 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 17 / 160 (10.63%) | 47 / 189 (24.87%) | 48 / 191 (25.13%) |
| occurrences (all) | 29 | 88 | 97 |
| Tooth infection | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 11 / 189 (5.82%) | 10 / 191 (5.24%) |
| occurrences (all) | 2 | 24 | 10 |

| | | | |
|------------------------------------|-------------------|-------------------|-------------------|
| Sinusitis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 6 / 189 (3.17%) | 18 / 191 (9.42%) |
| occurrences (all) | 1 | 7 | 24 |
| Pneumonia | | | |
| subjects affected / exposed | 6 / 160 (3.75%) | 20 / 189 (10.58%) | 24 / 191 (12.57%) |
| occurrences (all) | 6 | 21 | 31 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 10 / 189 (5.29%) | 10 / 191 (5.24%) |
| occurrences (all) | 1 | 13 | 11 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 13 / 160 (8.13%) | 71 / 189 (37.57%) | 62 / 191 (32.46%) |
| occurrences (all) | 16 | 137 | 133 |
| Influenza | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 22 / 189 (11.64%) | 13 / 191 (6.81%) |
| occurrences (all) | 3 | 24 | 18 |
| Herpes zoster | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 4 / 189 (2.12%) | 24 / 191 (12.57%) |
| occurrences (all) | 4 | 4 | 27 |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 15 / 189 (7.94%) | 15 / 191 (7.85%) |
| occurrences (all) | 4 | 21 | 18 |
| Rhinitis | | | |
| subjects affected / exposed | 5 / 160 (3.13%) | 21 / 189 (11.11%) | 23 / 191 (12.04%) |
| occurrences (all) | 5 | 31 | 29 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 45 / 160 (28.13%) | 35 / 189 (18.52%) | 45 / 191 (23.56%) |
| occurrences (all) | 55 | 47 | 69 |
| Dehydration | | | |
| subjects affected / exposed | 11 / 160 (6.88%) | 5 / 189 (2.65%) | 12 / 191 (6.28%) |
| occurrences (all) | 14 | 7 | 18 |
| Gout | | | |
| subjects affected / exposed | 4 / 160 (2.50%) | 14 / 189 (7.41%) | 10 / 191 (5.24%) |
| occurrences (all) | 5 | 24 | 19 |
| Hyperglycaemia | | | |

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|-----------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed | 3 / 160 (1.88%) | 15 / 189 (7.94%) | 6 / 191 (3.14%) |
| occurrences (all) | 3 | 20 | 8 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 13 / 160 (8.13%) | 12 / 189 (6.35%) | 4 / 191 (2.09%) |
| occurrences (all) | 19 | 13 | 5 |
| Hypokalaemia | | | |
| subjects affected / exposed | 16 / 160 (10.00%) | 33 / 189 (17.46%) | 39 / 191 (20.42%) |
| occurrences (all) | 25 | 50 | 67 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 8 / 160 (5.00%) | 11 / 189 (5.82%) | 15 / 191 (7.85%) |
| occurrences (all) | 16 | 16 | 23 |
| Hyponatraemia | | | |
| subjects affected / exposed | 6 / 160 (3.75%) | 7 / 189 (3.70%) | 4 / 191 (2.09%) |
| occurrences (all) | 6 | 8 | 5 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 3 / 189 (1.59%) | 9 / 191 (4.71%) |
| occurrences (all) | 4 | 8 | 10 |

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|--|---|--|--|
| Non-serious adverse events | Ixazomib+ LenDex (Exposure Up to 18 Cycles) | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 162 / 163 (99.39%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 7 | | |
| Hypotension | | | |
| subjects affected / exposed | 17 / 163 (10.43%) | | |
| occurrences (all) | 19 | | |
| Haematoma | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Flushing | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 5 | | |
| Deep vein thrombosis | | | |

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|--|-------------------|--|--|
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences (all) | 5 | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 30 / 163 (18.40%) | | |
| occurrences (all) | 53 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 8 / 163 (4.91%) | | |
| occurrences (all) | 8 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 66 / 163 (40.49%) | | |
| occurrences (all) | 91 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 4 | | |
| Malaise | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 6 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |
| subjects affected / exposed | 41 / 163 (25.15%) | | |
| occurrences (all) | 61 | | |
| Chills | | | |
| subjects affected / exposed | 11 / 163 (6.75%) | | |
| occurrences (all) | 14 | | |
| Asthenia | | | |
| subjects affected / exposed | 36 / 163 (22.09%) | | |
| occurrences (all) | 47 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

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|-----------------------------|-------------------|--|--|
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 3 | | |
| Productive cough | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences (all) | 3 | | |
| Hiccups | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 4 | | |
| Epistaxis | | | |
| subjects affected / exposed | 7 / 163 (4.29%) | | |
| occurrences (all) | 8 | | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 8 / 163 (4.91%) | | |
| occurrences (all) | 11 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 21 / 163 (12.88%) | | |
| occurrences (all) | 29 | | |
| Dysphonia | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences (all) | 5 | | |
| Cough | | | |
| subjects affected / exposed | 28 / 163 (17.18%) | | |
| occurrences (all) | 33 | | |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 4 | | |
| Anxiety | | | |
| subjects affected / exposed | 22 / 163 (13.50%) | | |
| occurrences (all) | 22 | | |
| Confusional state | | | |

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|--|-------------------|--|--|
| subjects affected / exposed | 16 / 163 (9.82%) | | |
| occurrences (all) | 19 | | |
| Irritability | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |
| subjects affected / exposed | 30 / 163 (18.40%) | | |
| occurrences (all) | 36 | | |
| Depression | | | |
| subjects affected / exposed | 18 / 163 (11.04%) | | |
| occurrences (all) | 19 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 2 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 6 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences (all) | 12 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 7 | | |
| Weight decreased | | | |
| subjects affected / exposed | 24 / 163 (14.72%) | | |
| occurrences (all) | 29 | | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences (all) | 4 | | |
| Fall | | | |
| subjects affected / exposed | 8 / 163 (4.91%) | | |
| occurrences (all) | 10 | | |
| Procedural pain | | | |

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|-------------------------------|-------------------|--|--|
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |
| Skin laceration | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 6 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 9 / 163 (5.52%) | | |
| occurrences (all) | 9 | | |
| Palpitations | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Nervous system disorders | | | |
| Tremor | | | |
| subjects affected / exposed | 14 / 163 (8.59%) | | |
| occurrences (all) | 18 | | |
| Syncope | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 4 | | |
| Sciatica | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 5 | | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 23 / 163 (14.11%) | | |
| occurrences (all) | 31 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 9 / 163 (5.52%) | | |
| occurrences (all) | 10 | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Memory impairment | | | |

| | | | |
|--------------------------------------|-------------------|--|--|
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 4 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 7 | | |
| Headache | | | |
| subjects affected / exposed | 15 / 163 (9.20%) | | |
| occurrences (all) | 21 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 9 / 163 (5.52%) | | |
| occurrences (all) | 12 | | |
| Dizziness | | | |
| subjects affected / exposed | 27 / 163 (16.56%) | | |
| occurrences (all) | 34 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 51 / 163 (31.29%) | | |
| occurrences (all) | 85 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 32 / 163 (19.63%) | | |
| occurrences (all) | 77 | | |
| Neutropenia | | | |
| subjects affected / exposed | 15 / 163 (9.20%) | | |
| occurrences (all) | 27 | | |
| Ear and labyrinth disorders | | | |
| Hypoacusis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |
| Vertigo | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences (all) | 3 | | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |
| Dry eye | | | |

| | | | |
|----------------------------------|-------------------|--|--|
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences (all) | 5 | | |
| Vision blurred | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 7 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 7 / 163 (4.29%) | | |
| occurrences (all) | 7 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 8 / 163 (4.91%) | | |
| occurrences (all) | 8 | | |
| Constipation | | | |
| subjects affected / exposed | 59 / 163 (36.20%) | | |
| occurrences (all) | 71 | | |
| Dental caries | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 68 / 163 (41.72%) | | |
| occurrences (all) | 115 | | |
| Nausea | | | |
| subjects affected / exposed | 55 / 163 (33.74%) | | |
| occurrences (all) | 77 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences (all) | 6 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 5 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|-------------------|--|--|
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 163 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry mouth | | | |
| subjects affected / exposed | 11 / 163 (6.75%) | | |
| occurrences (all) | 11 | | |
| Toothache | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences (all) | 4 | | |
| Stomatitis | | | |
| subjects affected / exposed | 10 / 163 (6.13%) | | |
| occurrences (all) | 10 | | |
| Vomiting | | | |
| subjects affected / exposed | 41 / 163 (25.15%) | | |
| occurrences (all) | 59 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 11 / 163 (6.75%) | | |
| occurrences (all) | 13 | | |
| Alopecia | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences (all) | 4 | | |
| Urticaria | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Rash papular | | | |
| subjects affected / exposed | 8 / 163 (4.91%) | | |
| occurrences (all) | 12 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 37 / 163 (22.70%) | | |
| occurrences (all) | 69 | | |
| Rash macular | | | |
| subjects affected / exposed | 11 / 163 (6.75%) | | |
| occurrences (all) | 27 | | |
| Rash erythematous | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 10 | | |
| Rash | | | |
| subjects affected / exposed | 11 / 163 (6.75%) | | |
| occurrences (all) | 11 | | |
| Pruritus | | | |
| subjects affected / exposed | 16 / 163 (9.82%) | | |
| occurrences (all) | 23 | | |
| Night sweats | | | |
| subjects affected / exposed | 9 / 163 (5.52%) | | |
| occurrences (all) | 10 | | |
| Erythema | | | |
| subjects affected / exposed | 11 / 163 (6.75%) | | |
| occurrences (all) | 14 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 18 / 163 (11.04%) | | |
| occurrences (all) | 24 | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |
| Neck pain | | | |
| subjects affected / exposed | 7 / 163 (4.29%) | | |
| occurrences (all) | 9 | | |
| Myalgia | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences (all) | 10 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 12 / 163 (7.36%) | | |
| occurrences (all) | 13 | | |
| Muscle spasms | | | |

| | | | |
|-----------------------------|-------------------|--|--|
| subjects affected / exposed | 15 / 163 (9.20%) | | |
| occurrences (all) | 21 | | |
| Joint swelling | | | |
| subjects affected / exposed | 7 / 163 (4.29%) | | |
| occurrences (all) | 7 | | |
| Bone pain | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 4 | | |
| Back pain | | | |
| subjects affected / exposed | 26 / 163 (15.95%) | | |
| occurrences (all) | 30 | | |
| Arthritis | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Arthralgia | | | |
| subjects affected / exposed | 23 / 163 (14.11%) | | |
| occurrences (all) | 31 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 9 / 163 (5.52%) | | |
| occurrences (all) | 13 | | |
| Pathological fracture | | | |
| subjects affected / exposed | 7 / 163 (4.29%) | | |
| occurrences (all) | 8 | | |
| Pain in jaw | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences (all) | 5 | | |
| Infections and infestations | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 3 | | |
| Bronchitis | | | |
| subjects affected / exposed | 13 / 163 (7.98%) | | |
| occurrences (all) | 14 | | |

| | | | |
|-----------------------------------|-------------------|--|--|
| Cystitis | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 19 / 163 (11.66%) | | |
| occurrences (all) | 33 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 10 / 163 (6.13%) | | |
| occurrences (all) | 14 | | |
| Tooth infection | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Sinusitis | | | |
| subjects affected / exposed | 5 / 163 (3.07%) | | |
| occurrences (all) | 5 | | |
| Pneumonia | | | |
| subjects affected / exposed | 7 / 163 (4.29%) | | |
| occurrences (all) | 7 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 13 / 163 (7.98%) | | |
| occurrences (all) | 16 | | |
| Influenza | | | |
| subjects affected / exposed | 3 / 163 (1.84%) | | |
| occurrences (all) | 3 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 4 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 163 (2.45%) | | |
| occurrences (all) | 4 | | |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 163 (1.23%) | | |
| occurrences (all) | 2 | | |

| | | | |
|------------------------------------|-------------------|--|--|
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 34 / 163 (20.86%) | | |
| occurrences (all) | 39 | | |
| Dehydration | | | |
| subjects affected / exposed | 10 / 163 (6.13%) | | |
| occurrences (all) | 13 | | |
| Gout | | | |
| subjects affected / exposed | 1 / 163 (0.61%) | | |
| occurrences (all) | 1 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 7 / 163 (4.29%) | | |
| occurrences (all) | 12 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 10 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 33 / 163 (20.25%) | | |
| occurrences (all) | 46 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 6 / 163 (3.68%) | | |
| occurrences (all) | 6 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 10 / 163 (6.13%) | | |
| occurrences (all) | 27 | | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 9 / 163 (5.52%) | | |
| occurrences (all) | 14 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|--|
| 09 August 2019 | The following changes were implemented as per Amendment 4: 1. Updated statistical procedures to modify the number of events for the final PFS analysis. 2. Clarified the statistical boundary for PFS at the second IA. 3. Clarified that REVLIMID or generic lenalidomide may be administered as part of the study treatment regimen. 4. Removed the requirement to document adverse events that require breaking the blind in the eCRF. 5. Updated the SAE reporting contact information in Japan to BI Medical. 6. Clarified the duration of new primary malignancy AE assessment. 7. Clarified the locations of study centers. |
| 09 July 2020 | The following changes were implemented as per Amendment 5: 1. Added language to clarify ongoing treatment of participants—participants should be moved off study and onto commercial supply of ixazomib and/or lenalidomide, if available, and otherwise kept on study. 2. Updated Schedule of Events. 3. Revised Study Period Definitions. 4. Added explanatory text to Study Objectives. 5. Added explanatory text to Study Endpoints. 6. Added explanatory text to Overview of Study Design and removed language regarding the previous Schedule of Events. 7. Revised information regarding the interim analyses in the Overview of Study Design. 8. Revised thrombocytopenia text in Management of Clinical Events. 9. Revised Blinding and Unblinding text. 10. Revised language in Preparation, Reconstitution, and Dispensing. 11. Added a sentence to Packaging and Labeling. 12. Added language in Storage, Handling, and Accountability. 13. Added language regarding alternative methods for administering study procedures/assessments when it is not possible for the patient to come to the study site due to extenuating circumstances (eg, due to the COVID-19 pandemic). 14. Removed or revised several study procedures. 15. Revised language regarding unscheduled visits. 16. Revised language regarding completion of treatment. 17. Revised language regarding completion of study. 18. Revised language regarding discontinuation of treatment with the study drug regimen, and patient replacement. 19. Revised language regarding withdrawal of patients from study. 20. Revised language regarding statistical and quantitative analyses. 22. Added language to Independent Review Committee section. 23. Added language to Procedures for Recording and Reporting Adverse Events and Serious Adverse Events. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported